

University of Groningen

Visualization and exploration of multichannel EEG coherence networks

Ji, Chengtao

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:

2018

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Ji, C. (2018). *Visualization and exploration of multichannel EEG coherence networks*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

INTRODUCTION

The brain is the most complex organ of the human body. Brain connectivity is the field of analyzing neurons (micro-scale) or brain regions (macro-scale) and the relationships between them [100]. Visualization of brain connectivity could provide significant insight for understanding the mechanism of brain function and a meaningful aid for diagnosis of brain disease.

In this thesis, we apply visualization methods to investigate connectivity properties of the human brain at both the static and dynamic level.

1.1 BRAIN CONNECTIVITY

Modern brain imaging modalities can produce a great number of brain connectivity patterns. In general, these brain connectivities can be classified into three major classes: structural connectivity, also called anatomical connectivity, which represents the physical connections between neurons or brain regions [52, 89]; functional connectivity which reflects temporal correlations between neuronal activities occurring between pairs of spatially connected or unconnected regions [33, 122] and effective connectivity which concerns the causal influence of one region on another and is largely based on specific interaction models [7, 39].

1.1.1 *Structural Connectivity*

Structural connectivity gives a meaningful insight into the architecture of the brain and describes the physical connections across all scales: from micro-scale of individual synaptic connections between neurons to macro-scale of inter-regional pathways between brain regions. Evidence shows that neurons and brain regions that are spatially close have a high chance to be connected while spatially remote connections are less likely to be so. The structural connection information can be extracted by various imaging techniques, such as electron microscopy (EM), light microscopy (LM), or magnetic resonance imaging (MRI).

Electron microscopy allows imaging of neuronal tissue at the micro (nanometer) scale and is the only imaging modality that can resolve single synapses [100]. However, it is not applicable to live cell imaging since it is labor-intensive and time-consuming. The connectivity between single neurons can be defined by average synapse densities in different brain regions [24]. Light microscopy allows imaging single neuronal cells at the meso-scale and identifying the major part of cells, such

as dendrites, somas, axons and possibly synaptic connections. Imaging the geometry of neurons enables researchers to identify different types of cells. Diffusion tensor imaging (DTI) is a magnetic resonance modality for measuring white matter connectivity *in vivo*. It obtains volumetric data with directional information of water self-diffusion by measuring the proton's state with extra magnetic field gradients. Connectivity between brain regions can be estimated by fiber tractography, where visualized lines reflect the major direction of neural fibers [10].

1.1.2 *Functional Connectivity*

Functional connectivity has been estimated using a measure of generalized synchronization between brain regions of interest (ROIs) under a specific condition. Functional connectivity can be seen as a statistical property that does not concern direct physical connections. This kind of connectivity mainly can be constructed at the macro-scale by the following four acquisition techniques: functional magnetic resonance imaging (fMRI), electroencephalography (EEG), magnetoencephalography (MEG), and positron emission tomography (PET).

fMRI measures time-dependent neural activity in the brain based on the BOLD (blood-oxygen-level dependence) effect [97]. The resulting BOLD signals are used to determine the functional connectivity between brain regions by measuring their temporal correlation. EEG records brain electrical potentials from electrodes attached to the scalp, while MEG measures magnetic fields outside the head induced by electrical brain activity. The connectivity between brain regions underlying electrodes can then be estimated by calculating similarities between the electrode signals according to several methods [30]. PET measures neural activities indirectly by detecting pairs of gamma rays emitted by a positron-emitting radionuclide. In general, brain connectivity can be defined as the temporal correlation between two neurophysiological activities in different brain areas [40].

All of the techniques are noninvasive but they have different advantages and disadvantages. For example, both EEG and MEG measure neuronal activity directly and have higher temporal resolution than fMRI and PET but lower spatial resolution.

1.1.3 *Effective Connectivity*

Effective connectivity describes the causal influence one element of a system exerts over another and the associated connectivity information. Effective connectivity can be extracted by all functional neuroimaging techniques mentioned in the previous paragraph [40, 41, 109]. Most effective connectivity measures depend on a model between the partici-

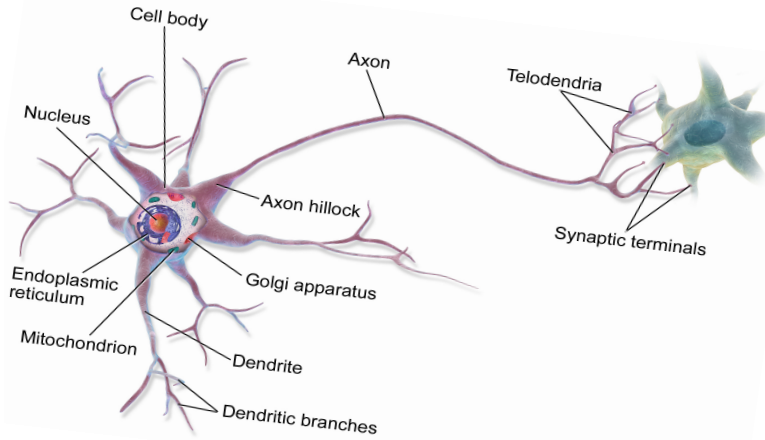


Figure 1.1: Schematic picture of two neurons. All neurons are electrically excitable, which means these cells receive, process, and transmit information through electrical and chemical signals. Source: <https://www.wikipedia.org/>.

pating regions, such as structural equation modelling, dynamic causal modelling, or Granger causality [15].

1.2 ELECTROENCEPHALOGRAPHY (EEG)

This section contains a more extensive introduction to the background of EEG, since this thesis focuses on functional connectivity derived from EEG data.

1.2.1 Brain potentials

Electroencephalography (EEG) measures the electrical potentials generated within the brain employing electrodes at the scalp during an EEG recording. To understand the nature of the voltages recorded by electrodes, it is necessary to understand the basic electrophysiological processes occurring within and between neurons (Figure 1.1). A typical neuron consists of a cell body, dendrites, and axon. The fundamental property of neurons is that they communicate with other cells via synapses, which are membrane-to-membrane junctions containing molecular machinery that allows rapid transmission of signals, either electrical or chemical [60].

There are two main types of electrical activity associated with neurons: action potentials and postsynaptic potentials [81]. Action potentials are discrete voltage spikes that propagate along the neuron's axon from the beginning of an axon towards the axon terminals (Figure 1.1).

This action potential triggers the release of neurotransmitter at the axon terminal of a neuron (the presynaptic neuron). Neurons communicate by these neurotransmitters. When the neurotransmitters bind to the receptors on the dendrites of another neuron (postsynaptic cell), it can cause a short-term change, for example, ion channels to open or close, leading to a change in the membrane potential called the postsynaptic potential.

The measured EEG is mainly generated by postsynaptic potentials and reflects the summation of both excitatory and inhibitory postsynaptic potentials. However, the human head is a conductive medium. Therefore, the electrical current spreads out through the head from the generator to the scalp. As a result of so-called *volume conduction*, the voltage recorded by electrodes will depend on the position and orientation of the generator and also on the resistance and shape of the various tissues (e.g., brain, skull, skin, and the scalp) of the head.

1.2.2 *Event-Related and Evoked Potential (ERP)*

The voltages recorded by electrodes can reflect the activity within the entire brain at the same moment in time because the speed of electrical transmission is very high. The event-related and evoked potential experimental designs, in which a large number of time-locked brain responses to repetitive stimulation are averaged, allows EEG researchers to investigate sensory, perceptual, and cognitive processing with millisecond precision [77].

1.2.3 *EEG Recording*

During an EEG recording session, electrodes are attached to the scalp at different locations. A conductive gel is applied between the skin and the electrodes to reduce impedance. Electrodes are typically positioned in fixed positions relative to the cerebral cortex, and each electrode has a label composed of letters and numbers to indicate its position (Figure 1.2). The letters present the brain regions (e.g., F for frontal), and the digits indicate lateralization (odd numbers for left, even for right) and distance from the midline (higher numbers are farther away) [98].

An electrical potential is measured from all electrodes simultaneously. The EEG will then be amplified for making it possible to be observed, and it can be filtered for removing artifacts. EEG can be studied during resting state or sleep, but in this thesis we focus on data acquired during an ERP experiment. In that case, after many trials, an averaging procedure is applied to extract the ERPs from the overall EEG.

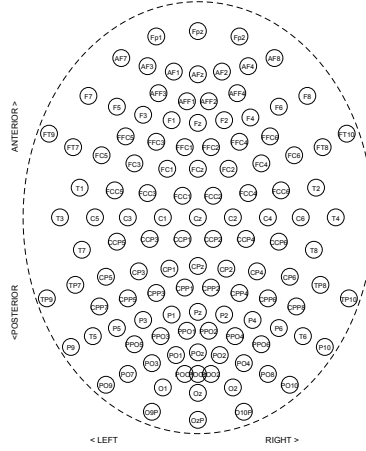


Figure 1.2: Locations (dots) and labels of 119 EEG electrodes as used for acquisition of data studied in this thesis, top view of the head. For nomenclature, see [98].

1.3 COMPLEX NETWORK ANALYSIS

In general, all forms of brain connectivity can be modelled as a network (also known as *graph* in the mathematical literature). A network, or graph $G = (V, E)$, is a set of nodes V and a set of links $E \subseteq V \times V$. Both structural and functional networks can be explored using existing graph theory by the following four steps [15, 107]:

1. Define network nodes. The nodes can be defined as electrodes or sensors in EEG or MEG studies [63, 86]. Parcellation schemes using prior anatomical criteria are also used to define nodes [120]. For example, in a functional network constructed by fMRI, the nodes typically correspond to anatomically localized regions.
2. Estimate the relationship between nodes. The relationships between nodes can take the form of any connectivity described in Section 1.1.
3. Generate a connectivity network. This network can be a weighted network, or a binary adjacency graph, i.e., unweighted network. The binary graph only shows the presence or absence of connections between nodes by applying a threshold to discard the connectivities below the threshold.
4. Calculate the network measures of interest. These parameters or topological features of a network can be used to describe the network. We will provide some measures in Section 1.3.2.

Exploring and analysing brain networks can shed light on the brain's cognitive functioning that occurs via the connections and interaction between neurons or regions. Since this thesis focuses on EEG coherence analysis, we will first introduce the multichannel EEG coherence network in Section 1.3.1. Computational analysis and interactive visualization are two common tasks for gaining insight into brain networks. Some widely used methods for analyzing networks are presented. Parameters used to measure the topology of a network will be briefly described in Section 1.3.2, and techniques used for visualizing networks will be given in Section 1.3.3.

1.3.1 Multichannel EEG Coherence Network

As mentioned before, a network, or graph $G = (V, E)$, consists of a set of nodes V and a set of links $E \subseteq V \times V$. An EEG coherence network is a special network in which nodes correspond to electrodes and links between these nodes correspond to coherences. If there are many electrodes, e.g., 64 or 128, the term “multichannel” or “high-density” EEG is used. Vertices, nodes, and electrodes are used interchangeably in this thesis, as well as links and edges.

The coherence c_λ as a function of frequency λ for two continuous time signals x and y is defined as the absolute square of the cross spectrum f_{xy} normalized by the autospectra f_{xx} and f_{yy} [53, 86]:

$$c_\lambda(x, y) = \frac{|f_{xy}(\lambda)|^2}{f_{xx}(\lambda)f_{yy}(\lambda)}.$$

EEG coherence is used to measure the synchronization between electrical activities recorded by electrodes attached at different sites. It can be regarded as the correlation between two electrode signals in the frequency domain.

1.3.2 Network Parameter Analysis

The functional organization of the brain is characterized by segregation and integration of information being processed [107].

A graphical model of brain connectivity is a convenient technique to formalize experimental findings. The topology of a network can be quantitatively characterized by its parameters. For brain network analysis, these parameters can be classified into two classes [107]: (i) parameters of functional segregation, which is the ability for specialized processing to occur within densely interconnected groups of brain regions; and (ii) parameters of functional integration, which is the ability to rapidly combine specialized information from distributed brain regions.

These parameters are often expressed in the following measures [15, 107]:

1. **Node degree:** the number of links connected to a node.
2. **Degree distribution:** the degrees of all nodes of a network.
3. **Associativity:** the correlation between the degrees of nodes that are connected by a link.
4. **Clustering coefficient:** the fraction of the node's neighbours that are also neighbours of each other.
5. **Motifs:** recurrent and statistically significant sub-graphs or patterns.
6. **Path length:** the minimum number of edges that must be traversed to go from one node to another.
7. **Efficiency:** measure of how efficiently a network exchanges information which is inversely related to path length.
8. **Connection density:** the actual number of edges in a network as a proportion of the total number of possible edges.
9. **Centrality:** the number of the shortest paths between all other pairs in the network that pass through a node.
10. **Hubs:** nodes with high degree or high centrality.
11. **Modularity:** Many networks can be divided into several modules (also called groups, clusters, or communities). Modularity is one measure of the structure of networks and is defined as the fraction of the edges that fall within the given groups of nodes minus the expected fraction if edges were distributed at random.

The description of parameters above is based on binary graphs. It can be easily extended to weighted graphs. For a detailed definition of these parameters please refer to [107].

1.3.3 Network Visualization

When researchers have well-defined questions to ask about their data, they can use purely computational analysis techniques. However, many analysis problems are not well-defined. For example, researchers often do not know in advance exactly how they want to analyze their data. In other situations, researchers want to see the structure of their data in more detail rather than having only a summarizing description. In these cases, interactive visualization methods employing the strengths

of the human visual system can help researchers to detect, understand, and identify unexpected patterns and outliers in their dataset.

For brain networks, although statistical and graph theoretical methods are available for brain network analysis (e.g., the parameters described above), network or graph visualization approaches can still provide important insights for the discovery of unanticipated patterns that would not be obvious through parameter analysis alone.

Based on the states of nodes and connections in the network, network visualization methods can be divided into static network visualization and dynamic network visualization.

1.3.3.1 Static Network Visualization

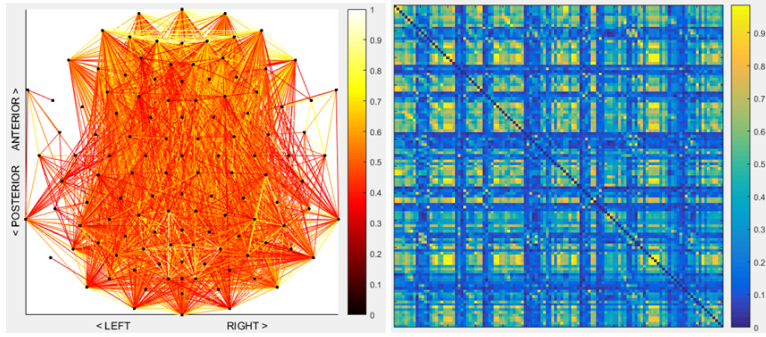


Figure 1.3: Two types of static network visualization techniques, employing data used in this thesis (see Chapter 2 for details). (a) Node-link diagram. (b) Matrix representation.

Visual representations of static graphs were reviewed by Landesberger et al. [75]. The most popular techniques used in visualizing networks can be divided into three main groups: node-link based, matrix-based, and hybrid.

The node-link diagram is the most common visual representation of a network. It has the advantages of intuitiveness, compactness, and suitability for understanding the network topology [47]. In this diagram, nodes are drawn as points and the connections between these nodes are drawn as lines (Figure 1.3(a)). The spatial position of the nodes can reflect their position in the brain. Size and color coding for nodes and edges is also very common. However, the node-link diagram suffers from scalability on limited displays, resulting in, for example, edge crossing and node overlap.

A network can also be represented by a matrix view, in which nodes are laid out along the vertical and horizontal edges of a matrix and connections between nodes are indicated by a coloured cell in the matrix that is the intersection between their row and column (1.3(b)). Not only

can the cell colour encode the connection information, the ordering of nodes along the rows or columns can also reveal substructures in the network. Compared to the node-link diagram, the matrix view is suitable for larger and denser graphs. However, there is still the difficulty for users to investigate a very large network and the topological structure of such a network. For example, for brain network analysis, the spatial location of nodes usually should be taken into consideration.

Sometimes a combination of these two techniques, the hybrid method, is used to overcome their individual limitations [57].

1.3.3.2 *Dynamic Network Visualization*

In dynamic networks, the structures of nodes and/or edges evolve over time. In [8], dynamic network visualization approaches are reviewed and divided into three categories based on the representation of time: animation based, timeline based, and hybrid techniques.

Animation, in which the time dimension is mapped to a simulated time, is a natural way to display the change of a dataset over time [8]. To highlight the change of networks, the major consideration in animation is to preserve the mental map which is the abstract structural information of a graph [34, 88, 125]. For example, in a node-link diagram, the position of nodes should be kept stable. However, it is difficult to focus on many items simultaneously and track changes over long time periods due to the limited capability of human perception.

A timeline-based representation, in which the time dimension is mapped to a spatial dimension, has the advantage of providing a better overview of the evolution of dynamic networks. However, it is limited by the size of the display screen and the dataset.

Interaction techniques are also assisting users to explore networks. Most common interaction approaches include zooming, panning, highlighting, and brushing and linking. In addition, specialized techniques have been developed for interactive visual network navigation and exploration.

1.3.4 *Visual Design*

The field of brain network visualization faces many challenges, e.g., the increasing quantity of data, the high dimensionality of data, and the question how to deal with spatially embedded brain networks [83, 99]. Determining the best visualization for all brain networks is difficult or may be even impossible.

Munzner proposed a nested model for visualization design and validation [90, 91]. This model consists of four stages: characterize the task and data by the domain vocabulary, abstract tasks and data, design visual encoding and interaction techniques, and create algorithms to execute techniques efficiently.

An applicable visualization should depend on the data structure and the desired tasks, which is the first level of the nested model. This stage needs a strong collaboration between designer and domain users. In order to understand the general problems the researchers are facing when analyzing their (fMRI/EEG) data, we used a questionnaire to collect requirements from a small group of researchers (see Chapter 2 for details). We analyzed the feedback and summarized four major requirements:

- **R1:** To compare brain activity under different conditions and identify differences. Most people want to investigate brain connectivity patterns under different conditions, e.g., during cognitive tasks or as a result of psychiatric disorders. One researcher wanted to use within- and between-individual variability in brain activation to explain differences in human behaviour. Another researcher wanted to investigate synchronization patterns and how such patterns relate to task conditions. In addition, researchers also wanted to investigate connectivity patterns within individuals.
- **R2:** To find the relationship between EEG phenomena or activities and brain regions. For example, one researcher wanted to localize pathological EEG phenomena and spontaneous brain rhythms. As far as visualization is concerned, one researcher wanted to see the link between nodes in the network and their anatomical location.
- **R3:** To analyze the dynamics in brain activity, for example, to analyze the differences in brain activity between the beginning and ending of a task.
- **R4:** To reduce the dimension of data. Two researchers mentioned that the main difficulty in visual analysis is that the data set is too large to visualize, which makes it is very hard to compare patterns.

1.4 THESIS CONTRIBUTION AND ORGANIZATION

The aim of this thesis is to develop and investigate methods to visually investigate brain connectivity determined by EEG coherence data. These methods in the following chapters are designed to satisfy some or all requirements mentioned in Section 1.3.4.

In Chapter 2, a design and implementation of a visualization framework for dynamic EEG coherence networks is presented. In this study, requirements for supporting typical tasks in the context of dynamic functional connectivity network analysis were collected from neuroscience researchers. These requirements cover **R1-R4** listed in the previous section. To satisfy these requirements, two visual representations

were provided: a timeline-based representation and a time-annotated functional unit (FU) map representation. The timeline-based representation is used to assist viewers to identify relations between functional connectivity and brain regions, as well as to identify persistent or transient functional connectivity patterns across the whole time window (**R2**, **R3**). The time-annotated FU map can facilitate the comparison of the behavior of nodes between consecutive time steps (**R1**, **R3**). Since both representations are based on the FU concept which divides all the nodes into several groups, this can be seen as a dimension reduction which is the aim of **R4**.

In Chapter 3, a method to enhance the identification of patterns in dynamic EEG coherence networks is proposed. In the timeline-based representation, it shows how FUs change over time: one FU may split into several FUs, several FUs can merge into one FU, FUs expand (shrink) when nodes join (leave) them, etc. However, relationships between FUs and their evolution pattern are not considered. The proposed method is implemented on the basis of the timeline-based representation by employing multidimensional scaling (MDS). It is used to find evolution patterns via the information of position marker and colour encoding (**R3**, **R4**).

In Chapter 4, a quantitative method for comparing brain connectivity between networks is proposed. In Chapter 2, the time-annotated FU map was used to visually compare FU maps. In this chapter, the proposed method quantifies differences among multichannel EEG coherence networks by performing a graph matching method based on the earth mover's distance (EMD) (**R1**). It accounts for the connectivity, spatial character and local structure at the same time. The method is applied to real functional brain networks for quantification of inter-subject variability during a so-called oddball experiment.

In Chapter 5, the method for the detection of FUs in EEG analysis is modified based on the community structure of an EEG coherence network. It partitions the set of electrodes into several data-driven ROIs (communities) based on their connections and positions (**R4**). As a result, electrodes within the same community are spatially connected and are more densely connected than electrodes in different communities. As an example application, the method is applied to the analysis of multichannel EEG coherence networks.

In Chapter 6, a summary and conclusions are presented, as well as suggestions for future research.

